

Table 1.1.2 Correspondence between Mode of Inheritance, Clinical Variation, and Genetic Heterogeneity for Selected Mendelian Disorders

Disorder	Mode(s) of inheritance ^a	Clinical variation		Heterogeneity	
		Familial	Nonfamilial	Allelic	Locus
Alzheimer disease	AD	Y	Y	?	Y
Charcot-Marie-Tooth disease	AD, AR, XD, XR	Y	Y	?	Y
Cystic fibrosis	AR	Y	Y	Y	N
Duchenne muscular dystrophy	AR, XR	N	N	Y	Y
Ehlers-Danlos syndrome I, II, and V	AD, XR	Y	Y	Y	N
Huntington disease	AD	Y	Y	Y	N
Marfan syndrome	AD	Y	Y	Y	N
Neurofibromatosis	AD	N	Y	Y	N
Tuberous sclerosis	AD	N	Y	?	Y
Usher syndrome, type I	AR	N	N	?	Y
Wilson disease	AR	Y	Y	?	N

*Abbreviations: AD, autosomal dominant; AR, autosomal recessive; N, no; XD, X-linked dominant; XR, X-linked recessive; Y, yes; ?, unknown.

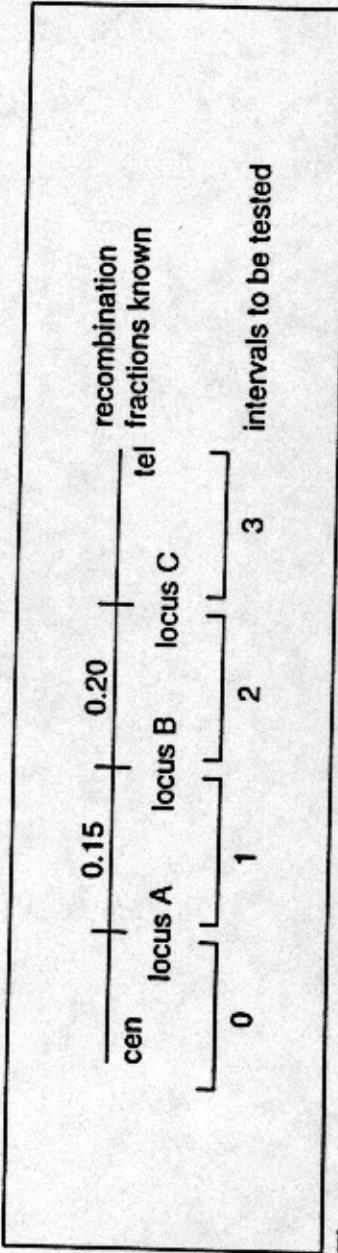


Figure 1.7.1 Genetic map showing recombination frequencies between markers A and B and between markers B and C, along with designation of each of the four intervals to be tested in a multipoint linkage analysis.

$$\text{multipoint lod score} = \log_{10} \frac{L(\text{Ped} \mid \theta_{A-B}, \theta_{B-C}, \theta_{\text{disease}=x})}{L(\text{Ped} \mid \theta_{A-B}, \theta_{B-C}, \theta_{\text{disease}=0.50})}$$

$$\text{multipoint lod score} = \log_{10} \frac{L(\text{Ped} \mid \theta_{\text{disease}-A=0.05}, \theta_{A-B=0.15}, \theta_{B-C=0.20})}{L(\text{Ped} \mid \theta_{\text{disease}-A=0.50}, \theta_{A-B=0.15}, \theta_{B-C=0.20})}$$

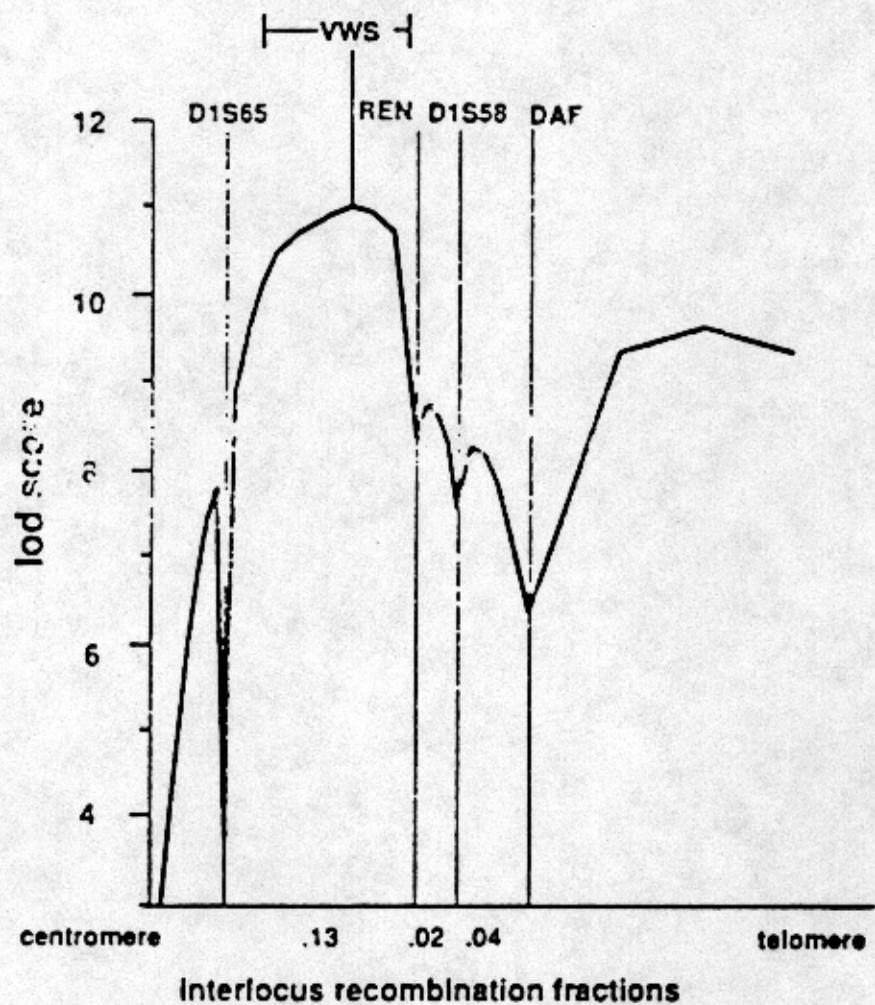
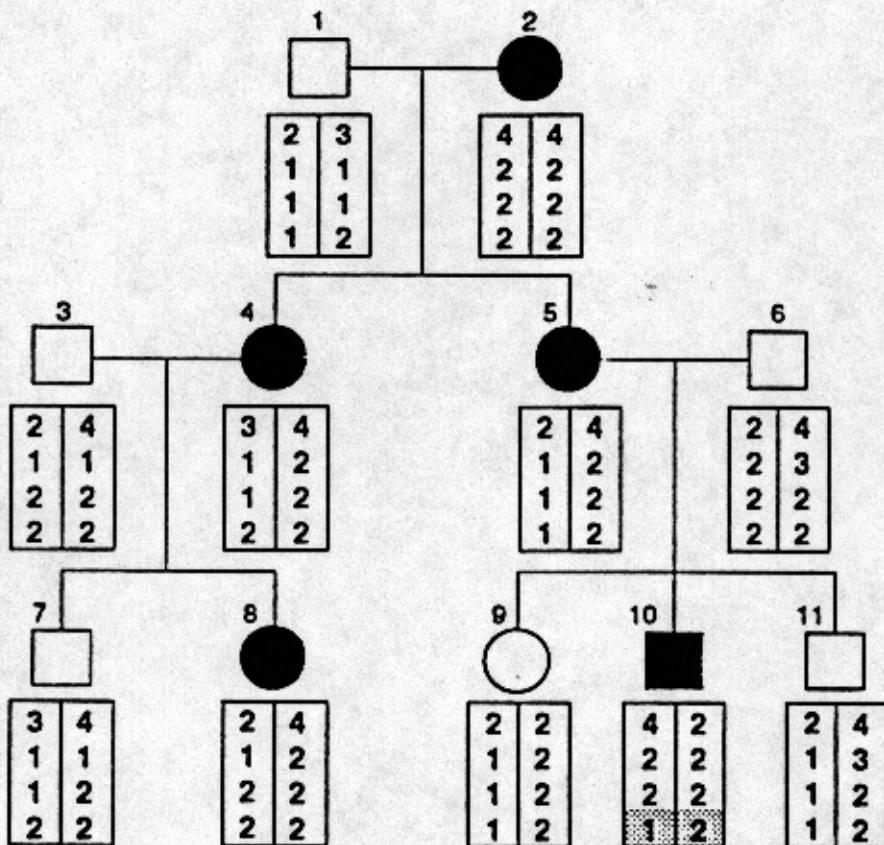


Figure 2 Results of location-score analysis of VWS for region surrounding REN. Brackets flanking VWS indicate 1-lod support interval. Anchor-map distances are presented as frequency of recombination for each interval.



pter →

A = 34
B = 12
C = 12
D = 22

cent →

chromosomal
haplotype

1, 2, 3, 4 = marker alleles

■ ● = affected individual

□ ○ = not affected

▨ = cross-over

CROSS-OVER:

individual #10: [(DISEASE-A-B-C)xo(D)]

Figure 1.4.6 Portion of a large disease pedigree depicting a key cross-over individual. Individual 10 is crossing over for marker D. Thus marker D defines a distal flanking marker for the disease in question, and the sequence of loci must be disease-A-B-C-(cross-over)-D.

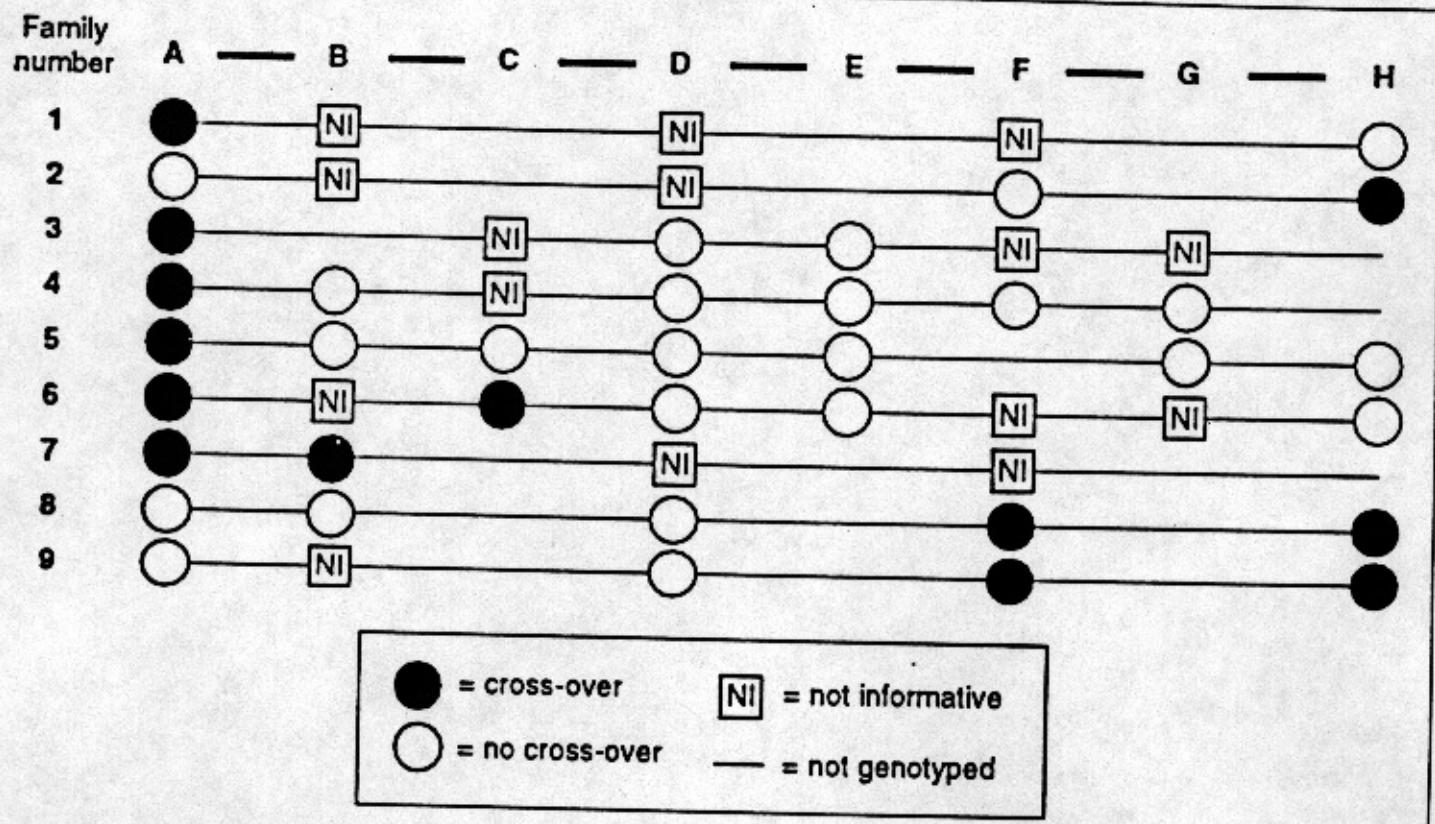


Figure 1.4.7 Method for summarizing all cross-over individuals in all family data used in a study. The most likely region for the disease gene is between markers C and F, the region where no cross-overs are found.

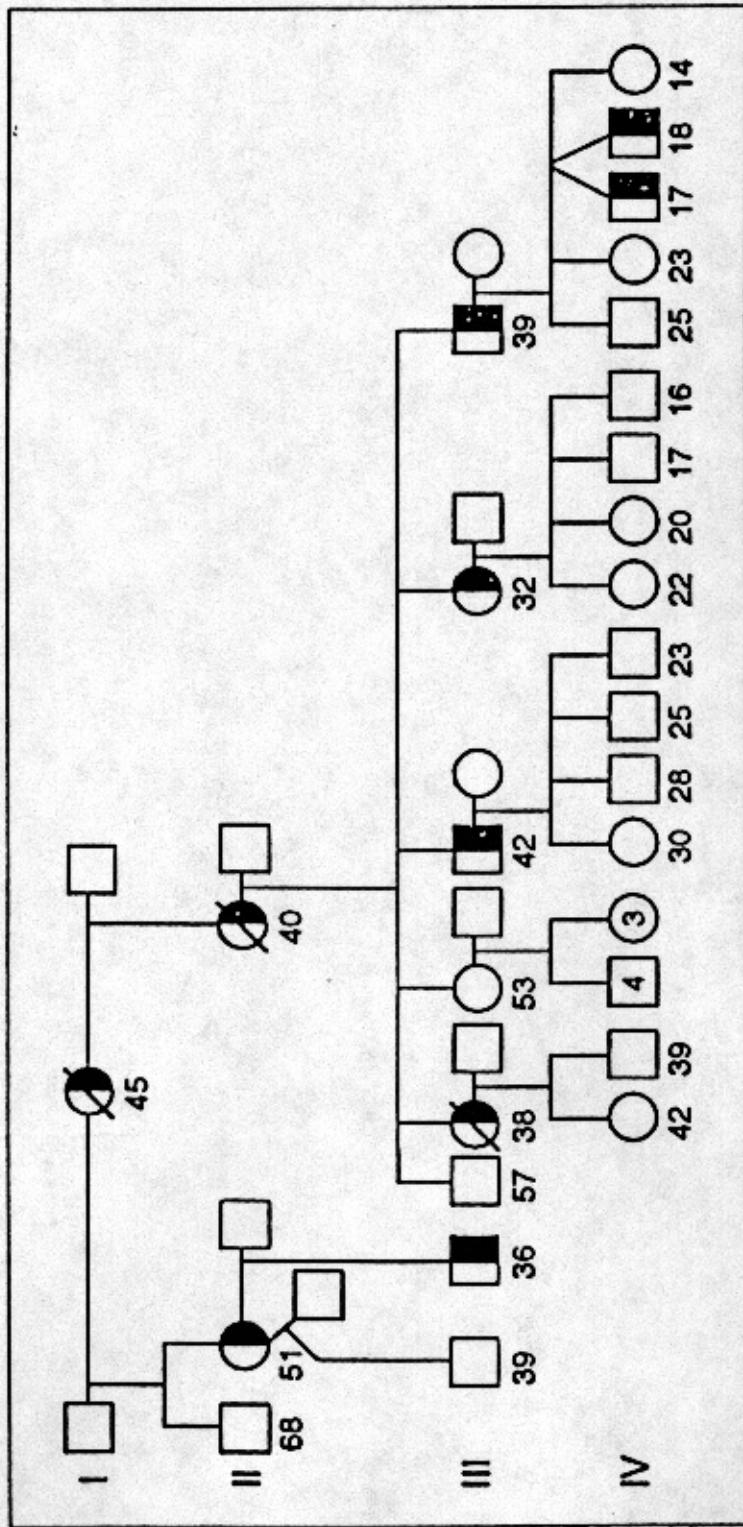


Figure 1.1.3 Pedigree of family with Huntington disease showing age-dependent penetrance. Few persons in youngest generation are affected because most HD gene carriers among them are not old enough to manifest symptoms. A half-shaded symbol indicates the person is affected. A slash through the symbol indicates that the person is deceased. Numerals within symbols represent multiple unaffected individuals of the same sex; numerals below symbols represent age at onset (for affected individuals) or age at last exam (for unaffected individuals).

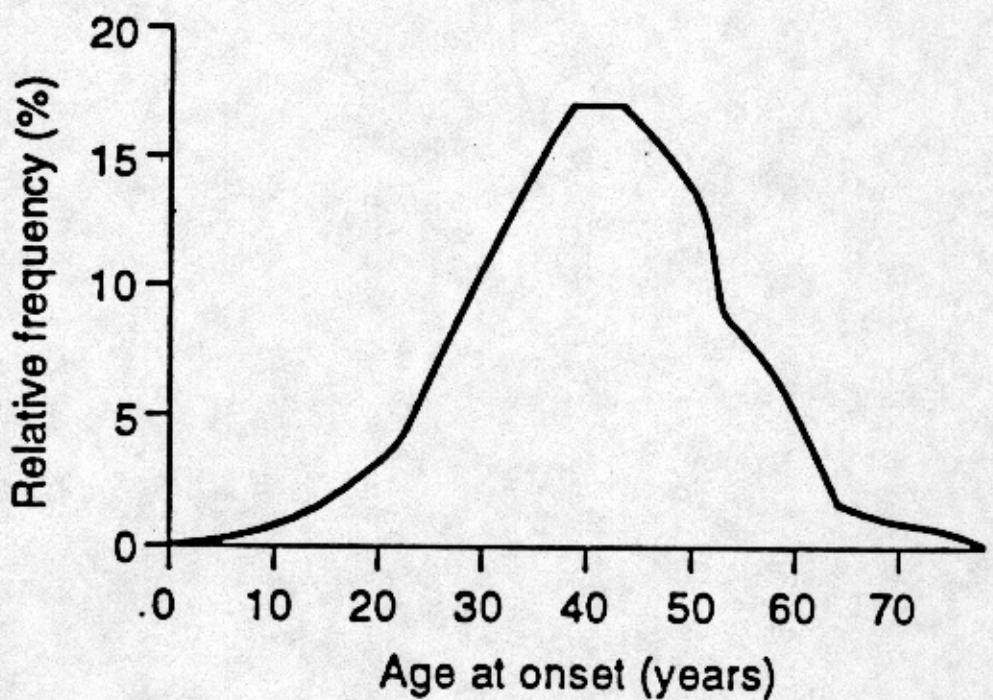


Figure 1.1.2 Distribution of age at onset in Huntington disease ($n = 610$). Percentage of total cases (relative frequency) is plotted against age at which they occur.
From Farrer, 1985.

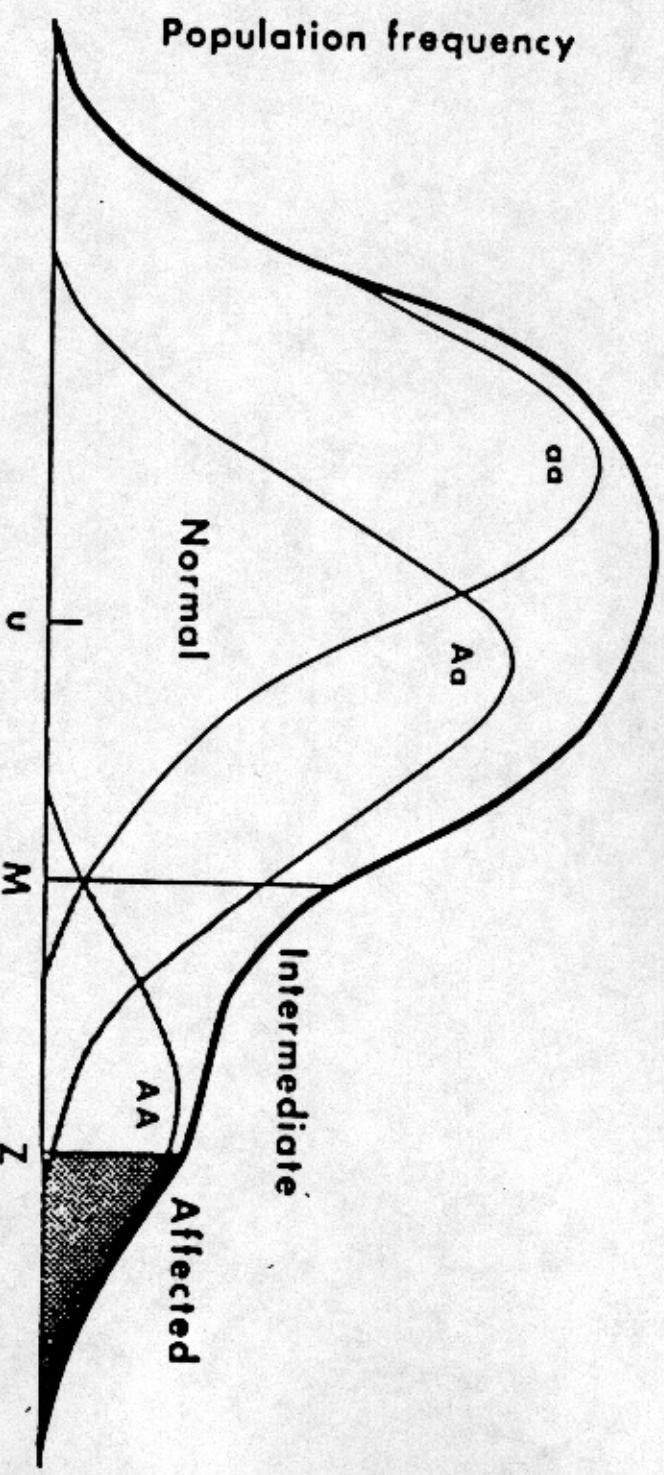


Fig. 5.5.1: The mixed model when the quantitative trait is trichotomized with affection excluded from intermediacy. M and Z are the two thresholds, and u is the mean.

$$\sum_{g_1} \cdots \sum_{g_N} \prod_{i=1}^N \Pr(Y_i | g_{c_i}) \Pr(g_{c_i})$$

Underlying etiology of a complex phenotype

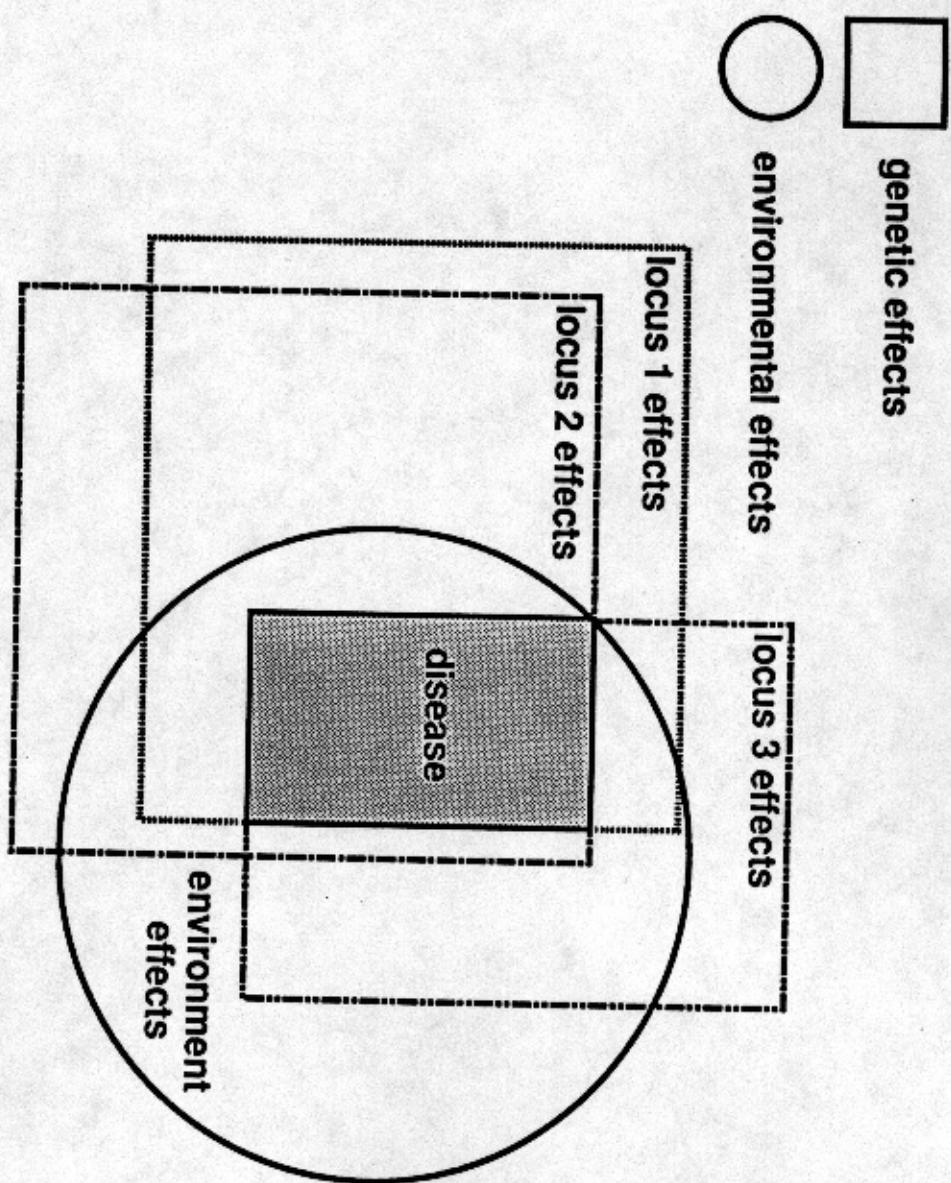


Table 1.1.3 Some Disorders Caused by Gene-Environment Interaction

Phenotype	Genotype	Environmental risk factor	Mechanism
Alcoholism	Alcohol dehydrogenase deficiency	Alcohol consumption	Genotype exacerbates effect of risk factor
Emphysema	α -1 antitrypsin deficiency	Smoking	Genotype and risk factor independently confer susceptibility
Heart disease	Familial hypercholesterolemia	High-cholesterol diet; lack of exercise	Genotype and risk factor independently confer susceptibility
Hemolytic anemia	G6PD deficiency	Fava bean consumption	Both genotype and risk factor required for expression
Malignant hypothermia	Malignant hypothermia	Anesthesia	Both genotype and risk factor required for expression
Skin cancer	Xeroderma pigmentosum	UV exposure	Genotype exacerbates effect of risk factor